

What is claimed is:

1. In a method of mixing a plurality of liquids comprising the steps of:

5 a) providing a probe tip with an internal cavity having a plurality of different inside diameters;

b) providing by aspiration a plurality of liquids inside a portion of the probe tip;

10 c) moving at least most of said liquids back and forth at least several times between a part of said cavity with a smaller inside diameter and a part with a larger inside diameter, said larger and smaller diameters being sufficient to provide a sufficient rotation of liquid as it moves between diameters to cause mixing of said liquids;

15 the improvement wherein the capillary number resulting from the mixing in said step c) does not exceed about 0.01, said capillary number being defined as the ratio of liquid velocity times viscosity and surface tension, so that any tails formed during said mixing step c) are minimized.

20 2. A method as defined in claim 1, wherein the capillary number of step c) does not exceed about 0.001, so that any entrained air bubble is more readily removed from said liquids as they are mixed.

25 3. A method as defined in claim 2, wherein said any bubble is aspirated into said probe tip in-between said plural liquids, with a volume that is less than that which prevents mixing of the liquids in the part of said cavity having the larger of said inside diameters.

30 4. In a method of mixing a plurality of liquids comprising the steps of:

a) providing a probe tip with an internal cavity having a plurality of different inside diameters;

b) providing by aspiration a plurality of liquids inside a portion of the probe tip;

5 c) moving at least most of said liquids back and forth at least several times between a part of said cavity with a smaller inside diameter and a part with a larger inside diameter, said larger and smaller diameters being sufficient to provide a sufficient rotation of liquid as it moves between diameters to cause mixing of said liquids;

10 the improvement wherein said cavity parts comprise two separate but mountable tip portions, and said method further includes the step of mounting a mountable tip portion of one of said inside diameters onto said tip portion of the other inside diameter in-between aspiration of liquids, such that carry-over contamination between liquids is prevented.

15 5. A method as defined in claim 4, and further including the steps of removing said tip portion after each additional liquid is aspirated, and attaching a new tip portion before aspirating into said probe tip an additional liquid.

20 6. A method as defined in claim 4, wherein said mountable tip portion has a larger inside diameter than that of said tip portion on which it is mounted.

25 7. A method as defined in claim 6, wherein said tip portion on which said mountable portion is mounted, further includes two inside diameters of significantly different values,

so that flow of said liquids past a demarcation zone between said differently valued inside diameters also provides rotational mixing of the liquids.

30 8. A method as defined in claim 7, wherein the larger of said differently valued inside diameters is at least as large as the largest inside diameter of said mountable tip portion.

9. A method as defined in claim 8, wherein said larger of said differently valued diameters is at least equal to three times the value of the smaller of said differently valued inside diameters.

5 10. A method as defined in claim 6, wherein the largest of said inside diameter of said mountable tip portion is at least equal to three times the value of the smaller of said differently valued inside diameters.

10 11. In a method of mixing a plurality of liquids comprising the steps of:

a) providing a probe tip with an internal cavity having a plurality of different inside diameters;

b) providing by aspiration a plurality of liquids inside a portion of the probe tip;

15 c) moving at least most of said liquids back and forth at least several times between a part of said cavity with a smaller inside diameter and a part with a larger inside diameter, said larger and smaller diameters being sufficient to provide a sufficient rotation of liquid as it moves between diameters to cause mixing of said liquids;

20 the improvement wherein said inside diameters are each a measure of a cross-sectional flow-through area of said cavity part, and the cross-sectional flow-through area of said larger inside diameter is at least three times the cross-sectional flow through area of said smaller inside diameter.

25 12. A method as defined in claim 11, wherein said one liquid is whole blood and wherein said moving step causes only mixing such that cells that have agglutinated are less likely to break apart.

30 13. In a method of mixing a plurality of liquids comprising the steps of:

a) providing a probe tip with an internal cavity having a plurality of different inside diameters;

b) providing by aspiration a plurality of liquids inside a portion of the probe tip;

c) moving at least most of said liquids back and forth at least several times between a part of said cavity with a smaller inside diameter and a part with a larger inside diameter, said larger and smaller diameters being sufficient to provide a sufficient rotation of liquid as it moves between diameters to cause mixing of said liquids;

the improvement wherein said larger inside diameter is obtained by i) selecting as a first tip portion a tapered tip at least a portion of which has an inside diameter that is much larger than the smaller inside diameter of the probe tip, and ii) joining said tapered tip to said probe tip having the smaller inside diameter using a joining collar mounted around said tip portion of step b).

14. In a method of mixing a plurality of liquids comprising the steps of:

a) providing a probe tip with an internal cavity having a plurality of different inside diameters;

b) providing by aspiration a plurality of liquids inside a portion of the probe tip;

c) moving at least most of said liquids back and forth at least several times between a part of said cavity with a smaller inside diameter and a part with a larger inside diameter, said larger and smaller diameters being sufficient to provide a sufficient rotation of liquid as it moves between diameters to cause mixing of said liquids;

the improvement wherein the total amount of liquid provided by said step b) is such that if all liquid is moved into said part with the larger inside diameter, the larger inside diameter is greater than the height of the total moved liquid, but less than twice the height of the total moved liquid, so that mixing as per step c) is maximized.

15. A method as defined in claim 14, wherein said mixing is accomplished without any substantial agitation or shaking of the probe tip.

16. In a method of mixing a plurality of liquids comprising the steps of:

5 a) providing a probe tip with an internal cavity having a plurality of different inside diameters;

b) providing by aspiration a plurality of liquids inside a portion of the probe tip;

10 c) moving at least most of said liquids back and forth at least several times between a part of said cavity with a smaller inside diameter and a part with a larger inside diameter, said larger and smaller diameters being sufficient to provide a sufficient rotation of liquid as it moves between diameters to cause mixing of said liquids;

15 the improvement wherein said step c) comprises moving at least most of the liquids back and forth at least between said cavity part with said smaller inside diameter and a part of said cavity of a larger inside diameter located at opposite ends of said cavity part of said smaller inside diameter, so that mixing efficiency is enhanced by rotation of the liquid as it moves past said opposite ends, rather than a single end of said smaller inside diameter cavity part.

20 17. A method as defined in claim 16, wherein said liquids are completely mixed within 7.5 repetitions of said movement back and forth at a flow rate of about 50 microliters per sec., within about 10 sec.

25 18. A probe tip for mixing liquids within the tip after aspiration of the liquids therein to, said tip comprising

30 a wall defining 3 connected cavities of unequal inside diameters one of the compartments being sandwiched as a middle compartment between the other two which form end compartments, each two adjacent cavities being connected by a transition zone wall and said inside diameters being sufficiently unequal in said adjacent 2 cavities as to cause rotational mixing of liquids as they move past said transition zone wall,

wherein said transition zone of the one cavity is formed by a variance of said inside diameter that increases in value as the middlemost cavity is transited outward into either of said other two end cavities.

5 19. A probe as defined in claim 18, wherein one of said end cavities is defined by a wall portion removably mounted on a wall defining said middle cavity.

10 20. A probe as defined in claim 19, wherein the inside diameter of at least one of said end cavities is at least equal to three times the value of the smaller of said differently valued inside diameters.

15 21. A method of determining the strength of an agglutination reaction within a hollow container comprising walls capable of transmitting light at certain predetermined wavelengths, comprising the steps of:

- 20 a) providing a mixture of a sample and an agglutinating reagent within a first cavity of the container, said cavity having a first inside diameter,
- b) transferring the mixture to a second cavity having a second inside diameter substantially smaller than said first inside diameter,
- c) scanning the liquid within said second cavity during said step b) with a beam of light at said predetermined wavelengths, said 10% portion being that portion closest to said first cavity;
- d) after said scanning step c), detecting the amount of light absorbed within or scattered by said 10% portion by said beam,
- e) transferring said mixture back into said first cavity,
- 25 f) repeating steps b)-d) at least once until some agglutinated material has separated from non-agglutinated material, and
- g) calculating the amount of agglutination from the absorbance or scattering detected in said step d).

30 22. A method as defined in claim 21, wherein said transfer step moves the liquid down from the first cavity to said second cavity, so that gravity assists in said separation of step f).

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23. A method as defined in claim 22, wherein said step g) comprises determining what percentage of the total possible absorbance is detected at a
5 preselected percent of the volume scanned that is indicative of agglutinating reactions, as an indication of the % and therefore the strength, of the agglutination that has occurred.

24. A method as defined in claim 21, wherein said detecting step d)
10 uses radiation at about 540 nm, the peak absorption wavelength of hemoglobin.

25. A method as defined in claim 21, wherein said step d) comprises
15 detecting the amount of scattered radiation, so that any hemolysis interference is avoided.

26. A method of agglutinating blood cells in whole blood, comprising
the steps of

a) aspirating whole blood into a disposable tip mounted on a probe, said tip
20 having at least two portions with significantly different inside diameters, connected to each other by a transition zone,

b) aspirating into the same tip thereafter, an agglutinating reagent, and

c) moving said blood and reagent back and forth as a total liquid, first entirely
25 into one of said portions and then entirely into the other of said portions, a sufficient number of times so as to cause coagulation of the cells of the whole blood, and then subsequent separation of plasma from the coagulated cells.

27. A method of separating as defined in claim 26, wherein said cells
30 are allowed to settle adjacent to an exit orifice of said tip, and d) thereafter, dispensing said cells out of said tip, leaving only plasma remaining therein.

28. A method of separating as defined in claim 27, and further comprising the step of e) dispensing at least a portion of said remaining plasma from said tip into a reaction well adapted for carrying out an immunoassay of the plasma.

5 29. A method of separating as defined in claim 26, wherein said agglutinating reagent is a polyelectrolyte or an antibody.

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